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10/562,324	06/29/2006	Gisela Greif	Le A 36 695	3066

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,324	GREIF ET AL.	
	Examiner	Art Unit	
	JAE W. LEE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *2 and 5-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

The previous amendment to claims, filed on 06/02/2008, is acknowledged, wherein Applicants have amended claims 1 and 13.

Claims 1-19 are pending in this application.

Priority

The instant application is the 371 national stage entry of PCT/EP04/07080, filed on 06/30/2004. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S. filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent application 103 30 235.2 (Germany) filed without English translation on 07/04/2003.

Election

Applicant's election of Group I, Claims 1, 3-5 and 13 in the response filed on 06/02/2008, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

It is noted by the Examiner that claim 13 will be withdrawn from further consideration on the merits because Applicants have amended the claim so that the vaccine no longer comprises the polynucleotide of Group I.

Claims 2 and 6-19 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Claims 1 and 3-5 will be examined on the merits.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Objections to the Specification

The specification is objected to for inappropriate notation of an Internet address. On page 38 line 32, and page 39 lines 1-4, Internet address is cited in an unacceptable form. See M.P.E.P. 707.05(e) for the acceptable notation of an Internet address. The examiner suggests the replacement of Internet citations with appropriate references because Internet pages are subjected to frequent changes and deletions and could be different when the public accesses the Internet page to view the exactly same information. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the

embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, Applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See particularly pages 34, 35, 37 of the specification containing nucleic acid sequences, and Figure 1 containing nucleic and amino acid sequences, and therefore, those sequences should be represented by proper sequence identifier numbers.

Appropriate correction is required.

Drawings

The drawings are objected to because labels for Figures 2 and 6, i.e., "Oocysten", "Kontrolle", "freie Sporozoiten", "Sporocysten mit Sporozoiten", etc. are in German, and not in English. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 1 and 5 are objected to because of the following informalities:

Claim 1 is objected to for reciting "a) ...; or b) ...; or c) ...; or". The Examiner suggests deleting all "or"s except for the one which should be inserted at the end of "d)".

Claim 1 is objected to because of the recitation, "b) a polynucleotide which exhibits an identity of more than 50% with the polynucleotide...," can be improved with respect to form. The Examiner suggests replacing the noted phrase with ---b) a polynucleotide which exhibits a sequence identity of more than 50% with the polynucleotide...---.

Claim 1 is objected to for the recitation of "the sequence [as] depicted in SEQ ID NO: X" because it can be improved with respect to form. The Examiner suggests replacing the noted phrase with ---the sequence of SEQ ID NO: X---.

Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of claims 2 and 4. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 2, 4 and 5 all encompass different subject matters.

Claim 5 is objected to for depending from a non-elected claim 2.

Claim 5 is objected to under 37 CFR 1.75(c) as being in improper form because it is multiply dependent from claims 2 and 4. See MPEP § 608.01(n). As such, Claim 5 will not be further examined on the merits.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3 and 4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claimed products, as written, does not sufficiently distinguish over the naturally occurring polynucleotides and cells in living organisms, i.e., *Eimeria tenella*. The claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of "the hand of man", the naturally occurring products are considered non-statutory subject matter. The Examiner suggests inserting "isolated" in front of "polynucleotide", "vector", and "host cell" to overcome this rejection. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980) and M.P.E.P. 2105.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3 and 4 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (3 and 4 dependent therefrom) is indefinite in the recitation of "stringent conditions" as this term is unclear absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. The art does not recognize a single set of experimental conditions as "stringent" and even the specification indicates that there are different degrees of stringency (e.g., "highly stringent", page 24, lines 15-17). While the specification has provided some conditions which are considered "stringent", these are merely exemplary conditions which do not define all the conditions intended to be "stringent". There is no specific definition in the specification of the term "stringent" or what constitutes "stringent conditions". For examination purposes, it will be assumed that the term "stringent conditions" reads "any hybridization conditions". Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for the polynucleotide as set forth in SEQ ID NO: 1, vectors and host cells comprising said polynucleotide, does not reasonably provide enablement for (A) any polynucleotide comprising: 1) any polynucleotide which exhibits a sequence identity of

more than 50% with the polynucleotide of SEQ ID NO: 1; 2) any polynucleotide which hybridizes, under any conditions, with the polynucleotide of SEQ ID NO: 1; 3) any polynucleotide which comprises any fragment of the polynucleotide of SEQ ID NO: 1 wherein said fragment is at least 6 nucleotides long, or 4) any polynucleotide which comprises any fragment of the polynucleotides of 1) or 2), wherein said fragment is at least 6 nucleotides long; (B) a vector or expression system which contains the polynucleotide of (A); or (C) a host cell which harbors the vector or the expression system of (B). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The disclosure of the specification is limited to the polynucleotide as set forth in SEQ ID NO: 3 which encodes the polypeptide as set forth in SEQ ID NO: 2, which can be used to stop the excystation of the sporozoites from the sporocysts, which is essential for the lifecycle of the parasite *Eimeria* (see page 8 of the specification) by using antibody directed against said polypeptide. However, the scope of the claimed invention does not commensurate with such disclosure because claims are drawn to polynucleotides having a significant portion of their structure undefined for which no use has been provided. The claims as written encompass (A) any polynucleotide comprising: 1) any polynucleotide which exhibits a sequence identity of more than 50% with the polynucleotide of SEQ ID NO: 1; 2) any polynucleotide which hybridizes, under any conditions, with the polynucleotide of SEQ ID NO: 1; 3) any polynucleotide which comprises any fragment of the polynucleotide of SEQ ID NO: 1 wherein said fragment is at least 6 nucleotides long, or 4) any polynucleotide which comprises any fragment of the polynucleotides of 1) or 2), wherein said fragment is at least 6 nucleotides long, (B) a vector or expression system which contains the polynucleotide of (A), or (C) a host cell which harbors the vector or the expression system of (B).

With regard to claim 1 b), the total number of variants of a polynucleotide having a specific sequence identity can be calculated from the formula $N!x19^{A}/(N-B)!/B!$, where

N is the length in nucleic acids of the reference polynucleotide, A is the number of different nucleic acids one can substitute with, and B is the number of allowed substitutions for a specific % identity. Thus, for a variant of the polynucleotide of SEQ ID NO: 1 having 50% sequence identity to SEQ ID NO: 1, the total number of variants to be tested is $1186!x3^{593}/(1186-593)!/593!$ (SEQ ID NO: 1 has 1186 nucleic acids; 593 nucleic acids = 0.50x1186) or $2.7x10^{638}$ variants. In the instant case, while the argument can be made that the variants having the recited structural features can be made with techniques known to one of ordinary skill in the art, the entire scope of the claims has not been enabled by the teachings of the specification or the prior art in view of the fact that the specification is completely silent as to how one could use those species which meet the recited structural features but do not encode proteins having the same function as that of the polypeptide of SEQ ID NO: 2. As such, one of skill in the art is left with the task of testing an essentially infinite number of species to select those that encode proteins having the same activity as that of the polypeptide of SEQ ID NO: 2 and determine how one could use those that encode proteins having a different activity. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claims.

Similarly, it would require undue experimentation for one of skill in the art to determine which polynucleotides, out of an essentially infinite number of possible polynucleotides that hybridize to the SEQ ID NO: 1 under any conditions, or that comprise fragments of a polynucleotide encoding the polypeptide of SEQ ID NO: 2, would encode proteins having the same activity as that of the polypeptide of SEQ ID NO: 2, and how to use the polynucleotides which do not encode a protein having the same activity as that of the polypeptide of SEQ ID NO: 2. In addition, it would require undue experimentation to determine which of the polynucleotides encoding proteins comprising the recited fragments are suitable for expressing a protein/peptide that biologically mimics the structure of the polypeptide as set forth in SEQ ID NO: 2, in order to develop antibodies against the protein/peptide for the use as a vaccine to stop the excystation of the sporozoites from the sporocysts, which is essential for the lifecycle of the parasite *Eimeria*. It is noted by the Examiner that since SEQ ID NO: 1 comprises non-coding DNA sequences on both N- and C-terminus of the coding sequence, without further guidance, one of skill in the art would not be enabled to use polynucleotides which comprise fragments from the non-coding regions to express a protein/peptide that biologically mimics the structure of the polypeptide as set forth in SEQ ID NO: 2, in order to develop antibodies against the protein/peptide for the use as a vaccine as explained above.

Because proteins having very different structures can have the same function (Kisselev et al, 2002), while proteins having very similar structure can have different

activities (Witkowski et al, 1999; Wishart et al, 1995), it would require undue experimentation for one skilled in the art to make and use the claimed products.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any polynucleotides and fragments thereof as explained above having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3 and 4 are rejected under 35 U.S.C. § 102(b) as being anticipated by Andrews et al. (US Patent No. 5,187,080, 1993).

The instant claims are drawn to (1) a polynucleotide comprising: a) the sequence of SEQ ID NO: 1; b) a polynucleotide which exhibits a sequence identity of more than 50% with the polynucleotide of SEQ ID NO: 1; c) a polynucleotide which hybridizes, under any conditions, with the polynucleotide of SEQ ID NO: 1; d) a polynucleotide which differs from a polynucleotide comprising SEQ ID NO: 1 due to the degeneracy of

the genetic code; or e) a fragment of a polynucleotide as described in a) to d) which is at least 6 nucleotides in length, (2) a vector or expression system which contains at least one of the polynucleotides of (1), and (3) a host cell which harbors the vector or the expression system of (2).

Andrews et al. specifically teaches the genomic DNA library of *Eimeria tenella,* vector and host cell comprising said genomic DNA (see Example 6 in column 21), It is noted by the Examiner that Applicants obtained the polynucleotide sequence of SEQ ID NO: 1 from the genomic DNA sequence of *Eimeria tenella* according to Example 8 of the instant specification. As such, the genomic DNA of *Eimeria tenella* taught by Andrews et al. inherently comprises a polynucleotide comprising: a) the sequence of SEQ ID NO: 1; b) a polynucleotide which exhibits a sequence identity of more than 50% with the polynucleotide of SEQ ID NO: 1; c) a polynucleotide which hybridizes, under any conditions, with the polynucleotide of SEQ ID NO: 1; d) a polynucleotide which differs from a polynucleotide comprising SEQ ID NO: 1 due to the degeneracy of the genetic code; or e) a fragment of a polynucleotide as described in a) to d) which is at least 6 nucleotides in length, and therefore anticipates the claimed invention. It is also noted by the Examiner that the polynucleotides as claimed need not be "isolated".

The examiner has presented evidence to reasonably support the polynucleotide or fragment thereof of the prior art, which is encompassed by the claim. According to MPEP 2112.V, once a reference teaching a product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or

reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

Since the Office does not have the facilities for examining and comparing applicants' polynucleotide/fragment with the polynucleotide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the polynucleotide/fragment of the prior art does not possess the same material structural and functional characteristics of the claimed polynucleotide/fragment). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Conclusion

Claims 1, 3 and 4 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in this Office action to be fully responsive in prosecution.

The instant Office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on M-F between 10:30-7:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAE W LEE/

Examiner, Art Unit 1656

/Delia M. Ramirez/

Delia M. Ramirez, Ph.D.
Primary Examiner, Art Unit 1652